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RANKIN, HILL & CLARK LLP
925 EUCLID AVENUE, SUITE 700
CLEVELAND, OH 44115-1405

EXAMINER	
EBRAHIM, NABILA G	

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BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Application Number: 10/531,160
Filing Date: April 12, 2005
Appellant(s): SHEKUNOV ET AL.

Randolph E. Digges
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed 12/20/07 appealing from the Office action mailed 7/26/07.

(1) Real Party in Interest

A statement identifying by name the real party in interest is contained in the brief.

(2) Related Appeals and Interferences

The examiner is not aware of any related appeals, interferences, or judicial proceedings which will directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal.

(3) Status of Claims

The statement of the status of claims contained in the brief is correct.

The appellant's statement of the status of amendments after final rejection contained in the brief is correct.

(4) Status of Amendments After Final

The appellant's statement of the status of amendments after final rejection contained in the brief is correct.

(5) Summary of Claimed Subject Matter

The summary of claimed subject matter contained in the brief is correct.

(6) Grounds of Rejection to be Reviewed on Appeal

The appellant's statement of the grounds of rejection to be reviewed on appeal is correct.

(7) Claims Appendix

The copy of the appealed claims contained in the Appendix to the brief is correct.

(8) Evidence Relied Upon

5,874,029	Subramaniam et al.	2/1999
6974593	Henriksen et al.	12/2005

(9) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

Claim Rejections - 35 USC § 103

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claim 1-7, and 15-21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Subramaniam et al. US 5,874,029 (hereinafter “Subramaniam”) in view of Henriksen et al. US 6974593 (hereinafter “Henriksen”).

Subramaniam teaches a method and an apparatus useful for the production of microparticles and nanoparticles.

The steps are:

Adding a solvent to a solute forming a mixture.

Adding the mixture to the SCF (which is a non-solvent)

Getting the particles out of the solute. (see abstract)

The invention can be used in the pharmaceutical, food, chemical, electronics, catalyst, polymer, pesticide, explosives, and coating industries, all of which have a need for small-diameter particles (abstract). The method comprises solutes such as drug, polymer, and/or excipient materials are solubilized. The supercritical antisolvent used is supercritical carbon dioxide (col. 6, lines 27, and 28), also a trifluoromethane is used (claim 12), which is encompassed by fluorocarbons recited in the current application, and poly-lactide glycolide copolymers (claim 22).

Subramaniam discloses the limitation recited in claim 8 regarding functional group of portion that is SCF-philic and SCF-phobic since the current specification discloses in paragraphs [0015 and 0027] that any compounds that comprise both SCF-philic groups, which make the compound soluble in SCF, and SCF-phobic groups, which have an affinity or attraction to the nuclei of the material(s) formed during the precipitation step, can be employed as growth retardant compounds. Examples of growth retardant compounds for use with supercritical carbon dioxide (SC--CO_2) include fluorocarbons. Accordingly, Subramaniam discloses a trifluoromethane, which is encompassed by the group of fluorocarbons. In addition the limitations recited in independent claim 15 of the instant application regarding expanding the SCF solution across a pressure drop below the critical pressure of the SCF whereby the SCF decompresses and causes supersaturation and nucleation of particles comprising the solute material, said particles having a smaller size and a reduced amount of agglomeration than if no growth retardant compound was present. Subramaniam discloses that following the drying period, the pressure is decreased to atmospheric level (col. 9, lines 11-24). Furthermore

Subramaniam teaches that accurate pressure control is essential in the highly compressible near-critical region. Pressure fluctuations in this region have a strong effect on the level of expansion of the organic solution and thus on the level of supersaturation and nucleation (col. 9, 25-29, col. 5, line 40, 41 and example 1).

Subramaniam is deficient in disclosing "growth retardant", such as sugar acetate, or block polymers.

Henriksen teaches particles of water insoluble biologically active compounds, particularly water-insoluble drugs, with an average size of 100 nm to about 300 nm, are prepared by dissolving the compound in a solution then spraying the solution into compressed gas, liquid or supercritical fluid in the presence of appropriate surface modifiers (abstract). Henriksen teaches a method that comprises (1) precipitating a compound by rapid expansion from a supercritical solution (Rapid expansion from supercritical solution) in which the compound is dissolved, or (2) precipitating a compound by spraying a solution, in which the compound is soluble, into compressed gas, liquid or supercritical fluid which is miscible with the solution but is antisolvent for the compound. In this manner precipitation with a compressed fluid antisolvent (Compressed fluid antisolvent) is achieved. Optionally, the process combines or integrates a phospholipid in water or other suitable surface modifiers such as surfactants, as may be required, into the processes. The surfactant is chosen to be active at the compound-water interface, but is not chosen to be active at the carbon dioxide-organic solvent or carbon dioxide compound interface when carbon dioxide is used as the supercritical solution (col. 2, lines 30+). Specifically, examples of suitable

second surface modifiers include one or combination of the following: block copolymers of ethylene oxide and propylene oxide and a tetrafunctional block copolymer derived from sequential addition of ethylene oxide and propylene oxide (col. 3, lines 37+).

Though Henriksen uses these compounds as surfactants and does not disclose literally "growth retardants", it is noted that provisional application 60475547 which Applicant claims priority to discloses the surfactant as alternative term for growth retardant (see specification pages 4, and 5).

Accordingly, it would have been obvious to one of ordinary skills in the art to use surfactants as polyethylene and polypropylene oxides to improve the outcome of the particles produced by micronization and nanonization of a solution containing insoluble active agent and organic solvent which is sprayed into compressed antisolvent because Henriksen discloses that to date of his invention, it has not been possible to make submicron particles by the compressed fluid antisolvent process without particle aggregation or flocculation. The objective is to overcome this limitation with the use of surface modifiers, also termed surfactant stabilizers (col. 5, lines 57+). The expected results would be a method of producing particles using a supercritical fluid which has less tendency to aggregate.

It is noted that the filing date of Henriksen is June 9, 2003 while the instant application claims benefit of 60/475,547 06/03/2003. However provisional 60/475,547 does not claim the copolymers recited in the instant claims. Provisional application 60/475,547 discloses polymers in the first paragraph only as follows:

> The current invention relates to a method of the formation of solid compositions using supercritical fluids. The solid compositions either consists of pure particles of a material/materials or particles of a coating material/materials (biodegradable polymer or lipid) having a pharmaceutical product encapsulated or adsorbed within its matrix. The current invention is highly suited for precipitation of non-agglomerated nanoparticles of pharmaceuticals or a blend of pharmaceuticals for drug delivery.

Accordingly, Henriksen is properly used in the rejection.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

> Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

2. Claims 1-7, and 15-21 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 9-13, 15, and 16 of copending Application No. 10/534,665, (application is now patent 7,279,181.)

Claims of application '665 recite the steps of mixing a solute in a solvent, contacting the solution with a liquefied gas (carbon dioxide), expanding the mixture to form droplets, and extracting the solvent to get the particles. The process includes sugars, or stabilizers, and the particles size range recited is within 0.05 to one micron (the ration recited in the current application is less than 10 micron and more than 300 nm which encompass the range recited in '665). Thus the instant claims are fully encompassed by the claims of the copending application.

3. Claims 1-21 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-6, 9-12, and 14-15 of copending Application No. 10/789422.

Application '422 recites a method of producing particles in which the steps are providing a supercritical fluid (carbon dioxide), two solvents, one is soluble in the SCF,

the other is substantially insoluble in the SCF and partially soluble in or miscible with the first solvent and a solute (active agent) which is soluble in the first solvent and is substantially insoluble in the second solvent and the supercritical fluid. Then contacting the two solvents with solute, then contacting the solution with SCF then precipitate the solute to extract the particles form the solvents. The process may include an excipient and the targeted particle size is between 10 micron and 10 nm (the range overlaps with the instant application disclosure). Thus the instant claims are fully encompassed by the claims of the copending application.

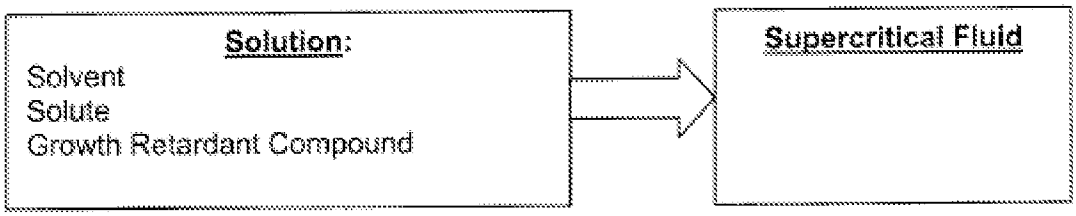
This is a provisional obviousness-type double patenting rejection.

(10) Response to Argument

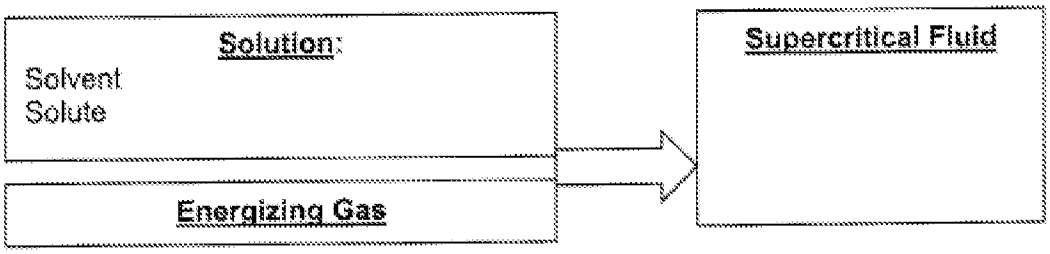
Appellant argues that:

In accordance with the invention as claimed in claim 1:

- a solution comprising a solvent, a solute and a growth retardant compound is provided;
- a supercritical fluid is provided; and
- the solution and the supercritical fluid are contacted together.



Subramaniam's method is significantly different from the method of instant claim1 and can be graphically depicted as follows:



Accordingly, Subramaniam does not ever disclose, teach or suggest that growth retardant compound should be mixed into the solution before the solution and the supercritical fluid are contacted together. Applicants explain to the Examiner that Subramaniam et al. mentioned trifluoromethane ("CHF3") once, and only in the context of trifluoromethane ("CHF3") being suitable for use as an SCF antisolvent (i.e., the material into which the solution is atomized, and not as a constituent of the solution), the Examiner stated that he did not find this persuasive. The Examiner did not explain why one having ordinary skill in the art would be motivated by Subramaniam et al.'s teaching

that trifluoromethane ("CHF3") can be used as a SCF to add trifluoromethane ("CHF3") to a solution that is contacted with a SCF.

To respond: Subramaniam's method comprises supercritical antisolvent which is supercritical carbon dioxide, trifluoromethane (claim 12), which is encompassed by fluorocarbons recited in the current application. Note that Subramaniam teaches that the solute and solvent mixture can be mixed with a compressed fluid (abstract), while claim 15 in the reference recites clearly that the compressed fluid can be trifluoromethane and a combination of gases, thus including the growth retardant compound. Finally, Henriksen discloses that a surface modifier can be used prior to the spraying step (claim 2).

Appellant argues that:

There is clearly no reason one skilled in the art would combine the teachings of Henriksen et al. with Subramaniam et al. Both accomplish the same goal (reduced particle size), but do so using different means.

To respond: because the two references are dealing with production of reduced particle size of insoluble drug or compound, they are considered analogous with the instant claims which are within the same scope. In addition, the motivation for combining is clear since it was obvious to one of ordinary skill in the art to use surfactants as polyethylene and polypropylene oxides to improve the outcome of the particles produced by micronization and nanonization of a solution containing insoluble active agent and organic solvent which is sprayed into compressed antisolvent because Henriksen discloses that to date of his invention, it has not been possible to make

submicron particles by the compressed fluid antisolvent process without particle aggregation or flocculation. The objective is to overcome this limitation with the use of surface modifiers, also termed surfactant stabilizers (col. 5, lines 57+). The expected results would be a method of producing particles using a supercritical fluid, which has less tendency to aggregate.

Appellant argues that:

Neither Subramaniam et al. nor Henriksen et al teach a process whereby a supercritical fluid is rapidly expanded across a pressure drop as claimed in claim 15. Appellant also argues that Henriksen includes supercritical fluid, a solute and optionally a co-solvent that are submitted to pressure drop. Instant claim 15 which recites a supercritical fluid, a solute and a growth retardant that are submitted to pressure drop.

To respond: Subramaniam teaches the use of triflurocarbon (growth retardant) before spraying. Further, Henriksen teaches the step of expanding SCF solution comprising a water insoluble solute across a pressure drop. The reference also discloses that the insoluble drug can be dissolved in a liquid and that it is not necessary for the stabilizer (surfactant, col. 5, lines 57+) to be soluble in carbon dioxide; it can be soluble in the liquid to be sprayed, as it only needs to be active at the carbon dioxide /solute interface (col. 6, lines 11+ and claim 16). Since the spraying step is in the same sequence as the spraying, then the disclosure reads on the instant claim 15.

(11) Related Proceeding(s) Appendix

No decision rendered by a court or the Board is identified by the examiner in the Related Appeals and Interferences section of this examiner's answer.

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

/Nabila G Ebrahim/

Examiner, Art Unit 1618

Conferees:

Hartley, Michael SPE 1618

/Michael G. Hartley/

/SREENI PADMANABHAN/

Supervisory Patent Examiner, Art Unit 1617

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